consideration. Lastly, Applicants wish to thank the Examiner for noting that the currently pending claims are free of the art.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 62 and 63 stand rejected under 35 U.S.C. §112, first paragraph, allegedly because the specification does not reasonably provide enablement commensurate with the scope of the claimed invention. The Office contends that Applicants' specification does not enable an isolated polypeptide that is at least 90% (or 95%) identical to the amino acid sequence of SEQ ID NO:299. The Office asserts that there is no guidance as to how to make the divergent sequences, that the molecules may possess functions that are not commensurate with the function of the native protein, and that such molecules may not maintain the activities proposed in the specification.

Applicants respectfully traverse this ground for rejection. Applicants wish to draw the Office's attention to the instant specification in which Applicants disclose many B305D isoforms (SEQ ID NOs: 306, 304, 305 and 315, for example) derived from B11Ag1, of which the polypeptide of SEQ ID NO:299 is one. These isoforms include sequences that share homology with the claimed polypeptide of SEQ ID NO:299 however, despite these sequence differences, all of these proteins share the similar characteristic of being over-expressed in breast tumor tissue (see page 34, for example). These disclosed B305D polypeptide sequences, in combination with the claimed polypeptide sequence of SEQ ID NO:299, can be used by one of skill in the art to identify amino acid residues that are suitable for substitution, deletion, or addition (see, for example, pages 10-14) that would not impact the breast tumor specificity of the sequence. The disclosed B305D sequences may be aligned with the claimed polypeptide sequence of SEQ ID NO:299 to identify conserved and/or variant amino acid residues between these various B11Ag1-derived sequences. Given that the disclosed sequences all share the same desired characteristic of breast tumor specificity, Applicants submit that the specification provides more than sufficient guidance to practice the claimed invention.

Furthermore, in the context of the current invention, the biological function of the claimed polypeptides is irrelevant to its over-expression in cancer tissue

relative to normal tissue and thus to its ability to be used, for example, in the detection of breast cancer. Rather, it is the breast-tumor expression profile of B305D isoforms described in the specification as filed, that is pertinent to the presently claimed polypeptides. Applicants submit that one skilled in the art, using only routine methodologies described in the instant specification (*e.g.* page 16, line 22 – page 20, line 30 and page 31, lines 5 - 30) and/or available within the general level of knowledge in the art, and without undue experimentation, could readily determine whether the claimed polypeptide compositions were either over-expressed in cancer relative to normal tissue, and/or could be used for the detection of breast cancer regardless of the biological function of the polypeptide. Moreover, Applicants submit that the skilled artisan would immediately appreciate that polypeptide sequences having 90%-95% identity to the amino acid sequence of SEQ ID NO:299 could readily be used to generate antibodies that crossreact with (*e.g.* recognize or bind to) a polypeptide comprising the amino acid sequence of SEQ ID NO:299, and thus be useful in such applications as diagnostics. Accordingly, Applicants urge that a skilled individual would readily appreciate, in light of the guidance set forth in the instant specification, and further in view of the level of general knowledge in this art, how to make and use the Applicants' claimed polypeptides without undue experimentation.

Applicants respectfully submit that the above comments obviate the rejection and request reconsideration and withdrawal of same under 35 U.S.C. § 112, first paragraph.

Claims 61-69 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Office asserts that the Applicants have not enabled use in immunotherapy nor identified immunogenic portions.

Applicants respectfully traverse this ground for rejection. Applicants wish to draw the Office's attention to Example 5, pages 40-41, and Figures 22-24 of Applicants' specification. Example 5 recites identification of four T-cell epitopes that are found within the claimed polypeptide sequence of SEQ ID NO:299: B11-8 (aa 29-37 of

SEQ ID NO:299), B11-1 (aa 231-238 of SEQ ID NO:299), B11-5 (aa 251-259 of SEQ ID NO:299) and B11-12 (aa 169-178 of SEQ ID NO:299). T cells were tested for peptide recognition using a standard ^{51}Cr release assay. T cells recognized the B11-1 peptide with strong recognition of the B11-8 peptide, see Figure 22. Clones from the CTL line described in the example were expanded and recognized the B11-8 peptide, see Figure 23, demonstrating that B11-8 is a naturally processed epitope. The T cells also recognize and lyse, in an HLA-A2 restricted manner, an established tumor cell line naturally expressing B11Ag1, see Figure 24. This indicates that the T cells recognize not only the peptide, but also recognized transduced cells and naturally expressing tumor cells, see page 41, lies 15-17. Applicants respectfully submit that the above comments obviate and overcome the rejection and request reconsideration and withdrawal of same under 35 U.S.C. §112, first paragraph.

On the basis of the above remarks, Applicants submit that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested.

Respectfully submitted,

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